REMARKS

Applicants thank the Office for the attention accorded the present Application in the July 30, 2002 communication.

Applicants have added new independent Claims 17 and 18, which are narrower apparatus claims. No new subject matter has been added. A check in the amount of $84.00 to cover the cost of the additional independent claims as the present application now contains a total of 12 claims with 5 independent claims.

35 USC §103(a) rejections:

Claims 1-10 were rejected under 35 U.S.C. §103(a) as being unpatentable over Pearle, Carruthers et al., Abby et al., Oakley et al, and Behounek et al. in view of Rork et al. Applicants respectfully traverse.

The Office states that the references Pearle, Carruthers et al., Abby et al., Oakley et al., and Behounek et al. do not expressly teach the incorporation of beta-blockers such as timolol, metoprolol, atenolol, and propranolol, and HMG-CoA reductase inhibitors such as pravastatin, folic acid, vitamin B6, and vitamin B12 into a single once-a-day dosage unit.

The Office cites Rork et al. for the proposition that Rork et al. teaches a sustained release system that can include beta-blockers such as timolol, metoprolol, atenolol, and propranolol and statin cholesterol lowering agents such as simvastatin, pravastatin, and lovastatin. The Office then concludes that it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate beta-

blockers such as timolol, metoprolol, atenolol, and propranolol with HMG-CoA reductase inhibitors such as pravastatin, folic acid, vitamin B6, and vitamin B12 into a single once-a-day dosage unit. However, Rork et al. do not teach a formulation containing more than a single active agent.

A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. See Dembiczak, 175 F.3d at 999, 50 USPQ2d at 1617. Close adherence to this methodology is especially important in cases where the very ease with which the invention can be understood may prompt one "to fall victim to the insidious effect of a hindsight syndrome wherein that which only the invention taught is used against its teacher." Id. (quoting W.L. Gore & Assocs., Inc. v. Garlock, Inc., 721 F.2d 1540, 1553, 220 USPQ 303, 313 (Fed. Cir. 1983)). Most if not all inventions arise from a combination of old elements. See In re Rouffet, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457 (Fed. Cir. 1998). Thus, every element of a claimed invention may often be found in the prior art. See id. However, identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. See id. Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant. See In re Dance, 160 F.3d 1339, 1343, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998); In re Gordon, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984).

The motivation, suggestion or teaching may come explicitly from statements in the prior art, the knowledge of one of ordinary skill in the art, or, in some cases the nature of the problem to be solved. See Dembiczak, 175 F.3d at 999, 50 USPQ2d at 1617. In addition, the teaching, motivation or suggestion may be implicit from the prior art as a whole, rather than expressly stated in the references. See WMS Gaming, Inc. v. International Game Tech., 184 F.3d 1339, 1355, 51 USPQ2d 1385, 1397 (Fed. Cir. 1999). The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art. See In re Keller, 642 F.2d 413, 425, 208 USPQ 871, 881 (CCPA 1981) (and cases cited therein).

Whether the Office relies on an express or an implicit showing, it must provide evidence that is clear and particular. See Dembiczak, 175 F.3d at 999, 50 USPQ2d at 1617. Broad conclusory statements standing alone are not "evidence." Id. Particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed. In re Werner Kotzab, 217 F.3d 1365, 55 USPQ2d 1313 (Fed. Cir. 2000).

In Kotzab, the invention involved an injection molding method for forming plastic articles. In particular, the invention involved the use of a single temperature sensor to control a plurality of flow control valves. The examiner cited a reference (Evans) for teaching that one system constructed and operated according to the applicant's invention may be used to control a number of valves. In view of this disclosure only,

the examiner concluded that the Evans reference teaches the use of one sensor to control a number of valves. This conclusion must necessarily rest on the unstated premise by the examiner that "one system" is equal to "one sensor." Id. at 1370.

Like Kotzab, the Office argues that because Rork et al. teaches that various agents may be used in the Rork delivery system and that beta-blockers and cholesterol-reducing agents are among the list of potential candidates that may be used, it necessarily follows that multiple agents may be combined into a single once-a-day dosage unit. (See Office Action dated July 30, 2002, Paper No. 6, Page 4, Paragraph 6 referencing Rork et al., col. 6, line 64-66 and col. 7, line 16). While the test for establishing an implicit teaching, motivation, or suggestion is what the combination of these two statements of Rork et al. would have suggested to those of ordinary skill in the art, the two statements cannot be viewed in the abstract. Kotzab at 1371. Rather, they must be considered in the context of the teaching of the entire reference. Further, a rejection cannot be predicated on the mere identification in Rork et al. of individual components of claimed limitations. Rather, particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed. Id.

Rork et al. discloses a controlled release nifedipine delivery device. Rork et al. discuss using their device for the delivery of a beneficial agent as a gelatinous dispersion consisting of (1) a core which contains a beneficial agent, a polymer which forms gelatinous microscopic particles upon hydration and, if desired, an agent to modulate the hydration of the polymer and (2) an impermeable, insoluble coating which

adheres to and surrounds the core and contains apertures which provide an area for the hydration and release of a dispersion comprising gelatinous microscopic particles. Rork et al. disclosed the use of only a single beneficial agent, i.e. one drug at a time, in their device. The use of the transition "consisting of" excludes the inclusion of a second beneficial agent within their delivery device. This is further evidenced by their definitions and the written description of the device.

Rork et al. defined "compressed core" as an admixture of **a** beneficial agent, a polymer and other ingredients that may affect any of the rate of production of dispersion, the stability of the components of the dosage form or the mixing or compression characteristics of the admixture. (Column 5, lines 4-10). The beneficial agent is **a** singular agent. Each time Rork et al. uses the term "drug" it is in its singular form, which connotes one drug. In fact, Rork et al. defined the term "drug" and its equivalents in the specification and the accompanying claims to include any physiologically or pharmacologically active substance (singular) that produces a localized or systemic effect. (Column 5, lines 21-25).

Rork et al. continues at Column 5, line 30 to say "**the** active drug", at Column 5, line 48 to say "**the** dissolved drug", at Column 7, line 33 to say "**the** drug can be", at Column 7, line 34 to say "also, **the** drug can be mixed", at Column 8, line 24 to say "the core compartment containing **the** drug", at Column 8, line 47 to say "in cases where **the** drug", at Column 8, line 55 to say "generally the core will contain 1% to 50% by weight, of **a** beneficial agent". In each instance, Rork et al. describe the drug as **a single** drug, not a combination of two beneficial agents combined together in a single dosage unit.

Every one of the 12 examples provided by Rork et al. contain only **on activ , beneficial agent** such as indomethacin (Examples 1-4), simvastatin (Examples 5 and 7), lovastatin (Examples 6, 8, 10 and 11), acetaminophen (Example 9), or nifedipine (Example 12). Every instance where a beneficial agent or drug is referred to, it is used singularly and **not** in combination with a second, different beneficial agent.

Rork et al. then list a large number of different drugs beginning in Column 5, line 63 to Column 7, line 17. Rork et al. provide this simply as list of various drugs that could be **individually** used in their device. Rork et al. disclosure is conspicuously absent of any examples of a formulation containing a beta-blocker and an antihyperlipidemic agent together in a single dosage unit.

When considered in the context of the teaching of the entire Rork reference as required by the Federal Circuit in Kotzab, there is not substantial evidence of record in Rork et al. to extrapolate this teaching to the combination of agents together in a single formulation dosage unit. Like the court's finding in Kotzab, at most, the combined teachings suggest that each agent may be delivered and released in situ and that one drug delivery device controls the in situ production and release of a dispersion containing a single, beneficial agent. As in Kotzab, there is not relevant evidence as a reasonable mind might accept as adequate to support the conclusion that, where there are a plurality of beneficial agents listed and each is capable of being delivered by a control release device, only one control release device provides the delivery for a plurality of beneficial agents together.

Furthermore, it cannot be said that there is such relevant evidence as a

reasonable mind might accept as adequate to support implicitly the conclusion that a skilled artisan confronted with (1) the problem noted by Dean et al., i.e. providing a combined single dosage regimen and method for reducing medication error and enhancing therapeutic compliance of combined medication agents for the treatment of cardiovascular disease, and (2) the list of beneficial agents in Rork et al., would have been motivated to reduce medication error and enhance therapeutic compliance of combined medication agents with a combination, single formulation dosage unit. In fact, Dr. Dean's declaration and supporting documents submitted earlier provide evidence of the then accepted wisdom in the field (i.e. reducing medication error and enhancing therapeutic compliance of combined medication agents is achieved by educating the physician regarding under-utilization of these medications and by educating the patient regarding compliance). An expert's affidavit of firsthand practical knowledge of unsolved needs in the art is evidence of the state of the art. In re Piesecki, 745 F. 2d 1468, 223 USPQ 785 (Fed. Cir. 1984).

Like Kotzab, the Office has fallen into the hindsight trap. The idea of a beta-adrenergic blocker and a cholesterol lowering agent that is a statin being combined as a single oral formulation as opposed to multiple agents being delivered by multiple oral formulations, is a technologically simple concept. With this simple concept in mind, the Office found prior art statements that in the abstract appeared to suggest the claimed limitation. But the Office points to no specific understanding or principle within the knowledge of a skilled artisan that would have motivated one with no knowledge of Dean et al.'s invention to make the combination in the manner claimed.

The same arguments are applicable to the subject matter claimed in new Claims 17 and 18.

In light of the above arguments, Applicants respectfully submit that Claims 1-10 and 17-18 of the present application contain patentable subject matter. Allowance of Claims 1-10 and 17-18 is therefore respectfully requested.

The Office is invited to telephone the undersigned if such communication would facilitate advancement of the present application and place it in condition for allowance.

Respectfully submitted,

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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231, on:

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